allow the best. Bipolar cauterization, the Falope Ring and the Pomeroy techniques offer an intermediary prognosis. The site of anastomosis is also pertinent to prognosis. An anastomosis between the cornu-isthmus or isthmus-isthmus yields the best results (a pregnancy rate of 70 percent to 75 percent). Poorer results (a pregnancy rate of 45 percent to 55 percent) are obtained when the anastomosis involves the cornu-ampulla or ampulla-ampulla.

When microsurgical techniques are used to reverse sterilization, intrauterine pregnancy rates of 58 percent and 65 percent have been reported in large series of patients by Winston and Gomel, respectively. In a smaller series (47 patients) followed for more than 18 months, Gomel reported a pregnancy rate of 81 percent. By comparison, *macro*surgical techniques for reversal of sterilization have resulted in 21 percent to 37 percent pregnancy rates.

Despite variations in technique, it is evident that microsurgical procedures for the reversal of sterilization in women offer substantially improved results.

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Antiprostaglandin Compounds in the Management of Primary Dysmenorrhea

WHILE THE EXACT incidence of dysmenorrhea is unknown, it appears to affect 30 percent to 50 percent of young women, causing them to lose time from work and school.

Primary dysmenorrhea occurs only in ovulatory cycles and is characterized by an absence of pelvic pathology and the presence of a variable number of systemic symptoms, including nausea, vomiting, diarrhea, headache, fatigue, dizziness and lower backache.

In the 1950's it was first suggested and subsequently proved that excessive prostaglandin action results in many of the symptoms of dysmenorrhea. In the early 1970's several papers were presented that indicated that nonsteroidal anti-inflammatory agents such as aspirin, indomethacin and naproxen, inhibited uterine contractions. Arachidonic acid is converted to prostaglandin through a number of steps. The first is the formation of a cyclic endoperoxidase. It is this step that is inhibited by the nonsteroidal anti-inflammatory drugs to prevent the production of excess prostaglandin.

A clearer understanding has been gained of the pathophysiology of dysmenorrhea and the efficacy of these inhibitors of prostaglandin synthesis in providing symptomatic relief, with the result that naproxen sodium and ibuprofen are among the drugs approved by the Food and Drug Administration for treatment of primary dysmenorrhea. Relief from symptoms is excellent for most patients, and these treatment compounds are well tolerated with minimal side effects. Most women who were formerly physically incapacitated by primary dysmenorrhea are now able to return to productive activity through use of these nonsteroidal anti-inflammatory compounds.

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A New and Effective Treatment of Hirsutism

HIRSUTISM, an androgen-dependent manifestation of accelerated hair growth, occurs in women having either ovarian or adrenal overproduction of androgens or hypersensitivity of hair follicles to androgenic stimulation (idiopathic hirsutism). In the past, satisfactory medical treatments have not been available. Recently, however, an understanding of the role of androgenic receptors in hair follicles combined with the characterization of several compounds that have antiandrogenic properties have afforded a new approach in the treatment of hirsutism.

Spironolactone (Aldactone), an aldosterone agonist, currently used as a diuretic and in the treatment of mild hypertension, has been found to possess several antiandrogenic properties. It has the ability to inhibit the cytochrome P-450 enzyme systems, which are required for the biosynthesis of androgens (by way of hydroxylation) in both the gonadal and adrenal steroid-producing cells and, consequently, result in reduced androgen secretion. It also inhibits the androgenic action of testosterone and its 5α-reduced metabolite, 5α-

dihydrotestosterone by occupying the binding sites of cytosol and nuclear receptors in all target tissues including hair follicles. Thus, the combined inhibitory effects on androgen production and action of spironolactone make it an ideal pharmacological agent for the treatment of hirsutism. Clinical trials by us and others have demonstrated that spironolactone reduces facial hair growth within three months with remarkable efficiency. A dosage regimen of 25 to 100 mg per day of spironolactone reduced testosterone and androstenedione production by 30 percent to 60 percent. Spironolactone is equally effective in idiopathic hirsutism and hirsutism due to ovarian androgen excess, such as in the polycystic ovary syndrome. These observations are consistent with the peripheral and glandular sites of action. Further, we have shown that the inhibition of androgen production is selective upon ovarian steroidogenesis and not upon adrenal steroidogenesis, which is an important consideration for long-term administration of spironolactone. In the long-term treatment (up to 16 months) of 30 patients during the past four years, we have not observed any significant side effects. Thus, it would appear that spironolactone is a safe and effective drug in the treatment of hirsutism.

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Severe Cardiovascular Complications Associated With β-Sympathomimetic Tocolysis and Their Prevention

TRANSIENT MYOCARDIAL ischemia, cardiogenic pulmonary edema and fatal myocardial insufficiency have been reported in association with β-sympathomimetic therapy for inhibition of preterm labor. The incidence of such severe cardiovascular complications is not known for most of these agents but is estimated to range from less than 1 percent for intravenously administered isoxsuprine (Vasodilan) to 5 percent for terbutaline (Brethine, Bricanyl) given intravenously. Because the causes of these complications are unknown, it is important to recognize several clinical features that characterize the development of cardiovascular compromise in these patients:

- Marked increase in cardiac work resulting from increased stroke volume and heart rate.
- The presence of multiple fetuses, which is known to be accompanied by increased plasma volume and cardiac output values.
- Excessive administration of fluids (crystalloids in particular) in the presence of fluid and sodium retention, resulting in decreased hematocrit and colloid osmotic pressure. This fluid retention is thought to be caused by activation of the renin-aldosterone axis.
- Hypokalemia without increased urinary potassium secretion, indicative of a shift of potassium into the intracellular compartment.
- Prolonged therapy—for at least 24 hours in most cases.
- Absence of correlation between the rate of drug administration and the development or severity of symptoms. Most patients have been treated with drug doses in the lower half of the accepted therapeutic spectrum.
- Prompt resolution of signs and symptoms after discontinuation of the drug, with or without induced diuresis.

Recently, the first β-sympathomimetic agent was approved by the Food and Drug Administration for use in the treatment of preterm labor; therefore, more patients will be exposed to possible severe adverse cardiovascular side effects of the drug. Physicians should include the following measures in the clinical management of patients receiving β-sympathomimetic tocolytic therapy:

- Monitor cardiovascular signs and symptoms frequently, especially in patients with multiple fetuses.
- Observe fluid balance carefully by accurately recording fluid intake and output as well as patient's daily weight (restrict fluid intake if fluid is retained).
- Avoid prolonged tachycardia (>140 beats per minute).
- If abnormal signs and symptoms develop, carry out tests such as an electrocardiogram, roentgenogram of the chest and echocardiogram before continuing therapy.
- Obtain baseline and follow-up blood specimens to monitor hemoglobin, hematocrit and electrolyte concentrations in patients receiving intravenous therapy.